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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09 576,057	05 23 2000	Joseph Chappell	07678-011004	3528

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EXAMINER

NASHED, NASHAAT T

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 02/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/576,057

Applicant(s)
Chappell et al.

Examiner
Nashaat T. Nashed

Art Unit
1652



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jan 13, 2003
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) | 6) <input type="checkbox"/> Other |

The application has been amended as requested in the communication filed January 13, 2003. Accordingly, claims 6-14 have been canceled and claim 4 has been amended

Claims 1-5 are under consideration as they relate to tobacco-*Hyoscyamus* CH4 chimeric isoprenoid synthase.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reasons set forth in the prior Office action, see paper number 9.

In response to the above objection, applicant traverse the compliance requirement on the ground that Figure 4A shows a series of schematic representation of chimeric isoprenoid synthase polypeptide, and Table 1 shows amino acid substitution at various position in the HVS or TEAS isoprenoid synthase. Also, they argue both Figure 4 and Table 1 each fail to disclose any nucleic acid and/or protein sequences.

Applicant arguments filed 1/13/03 have fully considered and they are found unpersuasive. Both Figure 4A and Table I contain references to specific nucleic and amino acid sequences, TEAS and HVS. Both Figure 4A and Table I refers to a specific amino acid residues in the amino acid sequence of TEAS (e. g., in Figure 4A, residues 152, 281, 379, and 442) and HVS (e. g., in Figure 4A, residues 160 and 268) without identifying the sequences from which these residues are derived. Table I refers to mutation of specific amino acid residues without identifying the amino acid sequence from which these residues are derived, see column 2 of the Table. The specification could not be comprehended without the amino acid sequences. In addition, Figure 4A contains a schematic diagram containing a restriction cites which presumably from a specific nucleic acid sequence. The application fails to teach the source of these particular nucleic acid sequences, and any attempts to produce these particular cDNA may result in isolating allelic variants which may not have the same restriction sites. While the applicants are not teaching any nucleic or amino acid sequences, Applicant invention is based on specific nucleic and amino acid sequences which are not described in the specification. Thus, the application contains disclosure of nucleic and amino acid sequences, and therefore, applicants must perfect their compliance with the sequence rules.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact

terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in the prior Office action, see paper number 9.

In response to the above objection, applicant traverse the rejection on the ground that they have described more than one species from the claims genus using TEAS and HVS, many isoprenoid synthases are known in the prior art, and a single species fulfill the written description requirement.

Applicant arguments filed 1/13/03 have fully considered and they are found unpersuasive. As indicated in the previous Office action, paper number 9, the specification teaches several chimeric polypeptides from TEAS and HVS synthases. Applicants have identified these chimeric polypeptide by cutting and pasting the nucleic acid sequences. There are no structural bases in the specification which would guide an ordinary skill in the art to generate other desired enzymatically active chimeric polypeptide from other synthase. There is no description of domain structure for the isoprenoid synthases which can be identifiable by sequence homology or by any other means in the prior art. In addition, the specification failed to identify specific structural domains with specific function whereby one of ordinary skill in the art could construct a desired functional chimeric isoprenoid synthase. Since specification failed to identify any structural bases for obtaining chimeric polypeptide synthase with desired activity, the number of known synthases is irrelevant. Clearly, other nucleic acid sequences encoding isoprenoid synthase would contain different restriction sites, and thus, the resulting chimeric polypeptide would not corresponds to any of those taught in the specification. The instant claims 1-5 are drawn to any chimeric polypeptide constructed presumably having any isoprenoid synthase activity without identifying any structural elements in the claims or identifying the particular activity of interest.

Claims 1-5 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to chimeric synthase produced by cutting and pasting the tobacco TEAS and *Hyoscyamus* HVS genes for the reasons set forth in the prior Office action, paper number 9.

In response to the above rejection, applicants argue that one skill in the art does not need to identify desired substrate specificities and that all is needed for an ordinary

skill in the art is to cut and past two polypeptides and detect activity by well know standard assays.

Applicants' arguments filed 1/13/03 have been fully considered but they are not deemed to be persuasive. The specification fails to provide adequate guidance to allow the skilled artisan to determine, without undue experimentation, which of the myriad possible combinations of fusing two polypeptides derived from different isoprenoid synthase to form chimeric synthase likely to retain catalytic activity. The specification provides only limited working examples of chimeric isoprenoid synthase, and the specification provides inadequate guidance regarding, for example, the domain structure of the various synthases, the location of the active site, or sites. In order to predict with reasonable assurance the effect that different chimeric protein are likely to have, at least a predictable enzymatic activity, and thereby predict which chimeric protein will retain catalytic activity, the skilled artisan would require data regarding, for example, the molecular basis of the enzyme's activity, its secondary and tertiary structure and the relative importance of any domains of the enzyme in maintaining said activity and substrate selectivity. The instant specification provides insufficient guidance to allow the skilled artisan to predict beforehand the effects of joining two fragments from two different isoprenoid synthase on the resulting activity. It is said all the ordinary skill in the art has to know to practice the claimed invention is to joins two different polypeptide fragments from two different synthase and assay for an activity, but one of ordinary skill in the art has to have a desired activity to assay for it. Since inadequate guidance is provided to allow prediction of the effect of joining fragments of two or more different enzymes on the resulting catalytic properties, determination of the full spectrum of the claimed chimeric synthase that would have a desired activity would require that the skilled artisan make and test a large number of all the possible chimeric proteins from joining one or more polypeptides from two or more synthases. Finally, applicants attention is directed to the fact the enablement requirement include specific or substantial utility which are neither taught or described in the specification. In another word, the ordinary skill in the art would need to know the use of individual chimeric synthase (a desired activity), or how to identify a chimeric polypeptide use before it is made.

Claims 1-5 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

- (a) The phrase "comprising a first isoprenoid synthase polypeptide joined to a second, different isoprenoid synthase polypeptide" in claim 1 render the claim indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired for the reasons set forth in the prior Office action, paper number 9.

- (d) claims 2-5 are included in these rejection because they are dependent on rejected claims and do not cure its deficiencies.

Applicants argue that the application defines isoprenoid synthase, and one of ordinary skill in the art would understand the meaning of chimeric isoprenoid synthase in light of said definition.

Applicants' arguments filed 1/13/03 have been fully considered but they are not deemed to be persuasive. The examiner disagrees with applicants argument. As indicated in the previous Office action, paper number 9, the "phrase isoprenoid synthase polypeptide" has an ambiguous meaning to one of ordinary skill in the art because the phrase have several meaning. Identifying the first and second polypeptide as "domains or fragments" of full length enzymatically active isoprenoid synthase would overcome this rejection.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 and 15-18 of U.S. Patent No. 5,824,774 ('774) for the reasons set forth in the prior Office action, paper number 9.

Applicants argue that they have filed a terminal disclaimer against the 774 patent, and therefore, the rejection should be vacated.

Applicants' arguments filed 1/13/03 have been fully considered but they are not deemed to be persuasive. No terminal disclaimer is filed.

No claim is allowed.

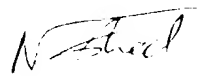
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday, and Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.


Nashaat T. Nashed, Ph. D.
Primary Examiner